IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Gokcen	Examiner:	Nickol, G.
Serial No.:	09/428,375	Group Art Unit:	1642
Filed:	October 28, 1999	Docket No.:	8004.4USC1
Title:	METHOD AND COMPOSITION FOR TREATING PROSTATE CANCER		

CERTIFICATE UNDER 37 CFR 1.10:
"Express Mail" mailing label number: EV 036303502 US
Date of Deposit: January 22, 2002

I hereby certify that this paper or fee is being deposited with the U S Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Commissioner for Patents, Washington, D.C. 20231.

By. _____
Name. Chris Stordahl

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

In response to the final Office Action mailed November 20, 2001, Applicant provides the following amendments and remarks.

In the Claims

Please cancel claims 1, 23 and 24 without prejudice.

Please add and consider new claims 33-58 as follows.

33. (NEW) A method of alleviating or curing a prostate tumor in a mammal comprising local administration to the prostate of a composition comprising therapeutically effective concentrations of collegenase and calcium ions.

34. (NEW) The method of claim 33, wherein the composition comprises about 1 mM to about 50 mM calcium ions.

35. (NEW) The method of claim 33, wherein the calcium ions comprise a calcium salt.

36. (NEW) The method of claim 35, wherein the calcium salt comprises calcium chloride.

37. (NEW) The method of claim 33, wherein the composition further comprises a therapeutically effective concentration of hyaluronidase.

38. (NEW) The method of claim 37, wherein the composition comprises about 1 mM to about 50 mM calcium ions, about 250 to about 250,000 U/ml collagenase and about 160 to about 160,000 U/ml hyaluronidase.

39. (NEW) The method of claim 33, wherein the composition further comprises a glycosidase, a protease, a nuclease, a lipase, an esterase, a streptokinase, or a combination thereof.

40. (NEW) The method of claim 33, wherein the composition further comprises an effective concentration of a nonionic surfactant.

41. (NEW) The method of claim 40, wherein the nonionic surfactant comprises Triton® X-100.

42. (NEW) The method of claim 33, wherein the composition further comprises an effective concentration of an antibiotic.

43. (NEW) The method of claim 42, wherein the antibiotic comprises gentamicin sulfate.

44. (NEW) The method of claim 33, wherein local administration comprises intraprostatic injection.

45. (NEW) The method of claim 44, wherein intraprostatic injection comprises intralesional injection, transurethral injection, transrectal injection, or transperineal injection.

46. (NEW) The method of claim 44, comprising administering a single injection of about 1 to 50 ml.

47. (NEW) The method of claim 44, comprising administering a single injection of about 1 to 5 ml.

48. (NEW) The method of claim 33, wherein local administration comprises administering a depot formulation.

49. (NEW) The method of claim 33, wherein local administration comprises administering a slow release implant, a microencapsulated composition, a conjugate with a biodegradable polymer, or a conjugate with a prostate-specific immunoglobulin.

50. (NEW) A method of alleviating or curing a prostate tumor in a mammal comprising local administration to the prostate of a sterile pyrogen-free solution comprising effective concentrations of calcium ions, collagenase, hyaluronidase, a nonionic surfactant, an antibiotic, and a pharmaceutically acceptable aqueous carrier having a physiologic pH; wherein the solution is suitable for administration to living mammals at single or multiple dosages of about 1 to 50 ml via intraprostatic injection; and wherein administration of said solution causes the necrosis, liquification, and regression of said tumor.

51. (NEW) The method of claim 50, wherein colleganase is provided at a concentration of about 2,500 to 25,000 U/ml.

52. (NEW) The method of claim 50, wherein hyaluronidase is provided at a concentration of about about 1,600 to 16,000 U/ml.

53. (NEW) The method of claim 50, wherein said solution further comprises a protease, a nuclease, a lipase, an esterase, a streptokinase, or a combination thereof.

54. (NEW) The method of claim 50, wherein the nonionic surfactant comprises Triton® X-100.

55. (NEW) The method of claim 50, wherein the antibiotic comprises gentamicin.

56. (NEW) The method of claim 50, wherein the intraprostatic injection comprises intralesional injection, transurethral injection, transrectal injection, or transperineal injection.

57. (NEW) The method of claim 50, comprising administering a single injection of about 1 to 20 ml.

58. (NEW) A method of alleviating or curing a prostate tumor of a living mammal comprising administering calcium ions to activate PSA in vivo.

REMARKS

Applicant has received and reviewed the final Office Action dated November 20, 2001. Claims 95-120 are pending in the application.

In the final Office Action, the Examiner rejected Claims 1-4, 6-23, 33-61 and 63-80 under 35 U.S.C. § 112, first paragraph, as not enabled by the specification. Applicant respectfully traverses the rejection. To further the prosecution of the application, and not to acquiesce to the rejection, Applicant has submitted herewith new claims 95-119. Applicant submits new claims 95-119 are supported by the specification. No new matter has been added.

In the final Office Action, the Examiner objected to the recitation in the claims of "a method of treating prostate cancer." To make the scope of claims abundantly clear, new independent claims 95 and 112 recite "a method of alleviating or curing a prostate tumor," which is supported and defined by the specification at least at page 3, lines 15-21.

The Examiner also based the enablement rejection on the recitation in the claims of various types of enzymes. In response, Applicant strongly urges that the specification provides ample guidance for including any of the enumerated enzymes in the composition of the invention when it is locally administered, as is recited in the claims. The specification provides in detail a discussion of the substrates acted upon and the mechanisms of each type of enzyme, for example on pages 5-9. One of skill in the art would readily appreciate that local administration of any of these enzymes would lead as readily to the degradation in the tumor of structural macromolecules as does collegenase. The skilled artisan would expect the effect of administering any of these enzymes directly to a tumor to be the same as adding them to a piece of tissue or cell culture *in vitro*. Therefore, Applicant asserts that it would not require undue experimentation to utilize any of these enzymes in the solubilization and breakdown of prostate tumor tissue. For these reasons, Applicants respectfully submit that the claims are in condition for allowance and notification to that effect is earnestly solicited.

CONCLUSION

In view of the remarks presented herein, pending claims 95-120 are in condition for allowance. Notification to that effect is earnestly solicited.

Respectfully Submitted,

MERCHANT & GOULD, P.C.
P.O. Box 2903
Minneapolis, Minnesota 55402-0903
(612) 332-5300

Dated: Jan 22, 2002

By: Mark T. Skoog

Mark T. Skoog
Reg. No. 40,178